

D<sup>3</sup> Claim 77. The composition of claim 73 that is effective for delivering said nucleic acid construct to heart muscle.

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**REMARKS**

Applicants filed an Amendment in the present application on February 14, 2000. On April 5, 2000, a telephone interview was held with the Examiner. The present Supplemental Amendment reflects the substance of that interview.

All of the issues in the application were discussed during the interview. The Examiner agreed that the submission of new claims 20-73 had addressed the issues regarding the form of the claims and rejections made under 35 U.S.C. § 101 and 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 112, first paragraph as to references in the claims to a "working model". Thus, the issues remaining to be resolved related to the rejection made under 35 U.S.C. § 112, first paragraph, for lack of written description support of a generic claim and enablement of the scope of "antisense or ribozymes" and prior art rejection.

**Written Description and Enablement**

With respect to the "antisense or ribozymes", Applicants presented arguments in their Amendment of February 14, 2000 essentially that the present invention is a vector for moving nucleic

acids into the body and targeting their action to a desired tissue. Applicants argued that the specification adequately describes for the skilled practitioner how to make the vectors and use them to move any desired nucleic acid into the desired target tissue. As to the nucleic acids actually moved, whether genes to be expressed, or antisense or ribozyme embodiments, one of ordinary skill in the art would be able to design effective embodiments of these elements and implement them using information known to the skilled practitioner. Thus, the specification need not describe these aspects of use of the invention.

The Examiner agreed that the argument was persuasive, but reserved the right to consider the matter more carefully before making a decision on the record.

The Examiner has also asserted that the claims are directed to pharmaceutical compositions and that the Applicant has not enabled therapeutic use of the invention. The Examiner's position is essentially that gene therapy has proven to be more expectation than success, and therefore, absent a demonstration of successful therapy, the Applicant has not enabled therapeutic use, as suggested by a "pharmaceutical composition." In the interview, it was discussed that amendment of the claims to recite a "composition" rather than a "pharmaceutical composition" would be remedial. This amendment has been made, and thus this ground of rejection overcome.

As discussed in the interview, Applicants further provide copies of articles of the periodical literature (Losordo et al., *Circulation* 98:2800 (1998) and Rosengart et al., *Circulation* 100:468 (1999)) that show that gene therapy has been successfully employed in treatment of myocardial ischemia (angina) by inducing heart muscle localized angiogenesis by overexpression of a vascular endothelial growth factor gene. In both instances the promoter used was a CMV promoter, thus constitutive and in this manner distinct from that of the present invention. The vectors employed in these studies were a plasmid DNA (Losordo) and a crippled adenovirus vector (Rosengart). Thus, Rosengart used a vector similar to that described in the present specification as to components other than the expression cassette. Applicants submit that the Losordo and Rosengart papers establish that gene therapy can be accomplished successfully using an adenovirus vector using a route of administration (injection into the heart cavity, see Losordo at p. 280, col. 1, lines 8-14) described in the specification (p. 21, paragraph 8).

As to the written description issue, the Examiner indicated in the Office Action that the specification did not describe a sufficient number of species of embodiments of the invention. The Examiner states that because the claims recited a "working model", the representative number of species required to support the generic claim was not clear. Applicants have argued that the specification

describes three different species of the invention: those carrying a gene to be overexpressed in the target tissue, those carrying a ribozyme, and those carrying an antisense construct. A working example is given of the embodiment of the gene to be overexpressed. All of these species are linked by the common structural characteristic of being nucleic acids and by the common functional characteristic that their expression (i.e., transcription into RNA) is desired in heart muscle tissue. Thus, the specification describes the generic invention in sufficient terms to show that the Applicants had possession of the claimed generic invention at the time the application was filed. Accordingly, the rejection of claims 1-19 under 35 U.S.C § 112, first paragraph, for lack of written description of the invention should not be applied to the present claims 20-77.

**Prior Art**

In the interview, the Examiner agreed that Franz is the closest of the primary references cited in making the prior art rejections. Applicants' Representative pointed out that the claims now recite that the inventive DNA fragment includes a MLE1 element, which is not specifically described in any of the references of record. The Examiner noted, however, that the Franz reference discloses a large DNA fragment that encompasses the smaller MLE1 element, though the

element is not specifically indicated. The Examiner should consider, therefore, that because the MLE1 element had not been identified in the prior art, there is no way it could be predicted *a priori* by one of ordinary skill in the art that the MLE1 element would be important to heart muscle-specific targeting of gene expression. The Examiner should also consider the limitation in dependent claim 21 that the claimed fragment lacks a CSS element. The combination of references cited by the Examiner does not disclose or suggest that heart muscle specific expression can be obtained by a vector comprising an MLE1 element in the absence of a CSS element. Furthermore, that such is the case would be considered unexpected by one of ordinary skill in the art in view of the references cited in making the prior art rejections of record. Note for example, p. 636, col. 1, lines 18-22 of the Franz reference cited by the Examiner.

For all of the above reasons, the new claims 20-77 should be found patentable over the prior art of record and the rejection of claims 1-19 under 35 U.S.C. § 103(a) should not be applied to the pending claims.

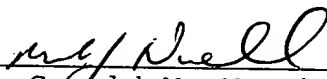
Applicants submit that the present application describes and claims patentable subject matter. Prompt, favorable action of allowance of the claims is respectfully requested. If there are any minor matters precluding allowance of the application which may be

resolved by a telephone discussion, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. (Reg. No. 36,623) at (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By   
Gerald M. Murphy, Jr.  
Reg. No. 28,977

Mark J. Nuell  
Reg. No. 36,623

P.O. Box 747  
Falls Church, Virginia 22040-0747  
(703) 205-8000

GMM/DRN/  
690-110P

Attachments: Losordo et al.  
Rosengart et al.